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PROCESS FOR IMPROVING ORAL HYGIENE AND DENTIFRICE COMPOSITION FOR ITS IMPLEMENTATION

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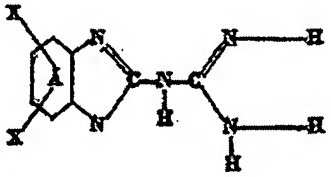
Agent:	Cabinet Lavoix

The present invention relates to a process making it possible to improve oral hygiene, and more particularly, to a process for inhibiting the formation of dental plaque. The invention also relates to effective compositions for improving oral hygiene and inhibiting the formation of dental plaque, compositions which essentially include a nontoxic support and an effective quantity of halogenated benzimidazolyl guanidine and/or salts of the aforementioned guanidine with nontoxic acids.

The essential active constituent of a composition which can be used for oral hygiene care in order to inhibit the formation of plaque, whether the composition is in the form of lozenges, strips, liquid gurgling solution or mouthwash, toothpaste or toothpowder, etc., is

2-(dihalobenzimidazolyl) guanidine and or one of its salts with nontoxic acids. The free base, 2-(dihalobenzimidazolyl) guanidine, can be represented by the formula:



in which X is chlorine, bromine or iodine and

is a C_6 aromatic nucleus.

Although various imidazoles, benzimidazoles, guanidines and bisguanidines have proven in many cases to have antimicrobial power, no simple germicide is known which, when used in topical applications in the buccal cavity, inhibits the formation of plaque. The 2-(dihalobenzimidazolyl) guanidines have the particular capability of being absorbed by the protein materials and of being released by them in vitro. It is this particular combination of properties to which the advantage of the 2-(dihalobenzimidazolyl) guanidines, with regard to improvement of oral hygiene and in particular inhibition of the formation of plaque, can be attributed.

The active substance, that is, 2-(dihalobenzimidazolyl) guanidine, in which the halogen is bromine, iodine or chlorine, and in which the benzene nucleus is substituted by identical or different halogens in position 5,6- or 4,5- or 4,6- or 4,7-, is presented in the form of lozenges or chewing strips, gargling solutions or mouthwashes, toothpaste or toothpowder, in which the active substance is in solution or in suspension, with it possible for said active substance to be associated with other active agents such as Na_2FPO_3, for example, as well as antibiotics, such as tylosine and desmycosine, in order to obtain a better effect.

The 2-(dihalobenzimidazolyl) guanidines are effective both in the form of free bases and in the form of salts formed with nontoxic acids. Currently, among the 2-(dihalobenzimidazolyl) guanidines, it is 2-(5,6-dichlorobenzimidazolyl) guanidine which is preferred. As an example of the power of the 2-(dihalobenzimidazolyl) guanidines, the effectiveness of 2-(5,6-dichlorobenzimidazolyl) guanidine will be mentioned, which, by daily application of solutions or suspensions of the free base, hydrochloride and hemimalonate, has been revealed to improve oral hygiene and in particular, to inhibit formation of plaque.

In a general manner, oral hygiene is improved by putting the buccal cavity in contact with a 2-(dihalobenzimidazolyl) guanidine, at an effective concentration of at least approximately 0.01% in a nontoxic vehicle. Thus, for example, a chewing strip essentially contains

approximately 0.1-2% or approximately 5-100 mg per strip of 2-(dihalobenzimidazolyl) guanidine [2-(5,6-dichlorobenzimidazolyl) guanidine being currently preferred], approximately 30-70% of a compatible abrasive (such as talc, chalk, alumina, insoluble sodium metaphosphate, insoluble dicalcium phosphate), approximately 30-50% of nontoxic moistener (such as mannitol, sorbitol, for example), approximately 0.5-3% of a substance putting the detritus in suspension (such as carboxymethylcellulose, Irish moss), approximately 1-3% of a nontoxic detergent (in particular a sarcosinate such as sodium N-lauroyl sarcosinate), approximately 5% of a binder such as polyethylene glycol (with a molecular weight of approximately 6000), approximately 1-2% of a lubricant for a matrix (such as magnesium stearate), as well as flavoring agents, coloring agents and sweeteners, to make 100%.

A solution for rinsing the mouth includes:

a. Approximately 0.01-0.5% 2-(dihalobenzimidazolyl) guanidine;

b. Approximately 0.5-1% of a nonionic nontoxic detergent, such as a product of condensation of polyoxyethylenated sorbitan monostearate containing approximately 60 mol ethylene oxide, [or] of a cationic detergent, such as a quaternary ammonium salt (for example, diisobutylphenoxyethoxyethyldimethylbenzylammonium chloride);

c. Sweetening, flavoring and coloring agents and aqueous alcohol to make 100%.

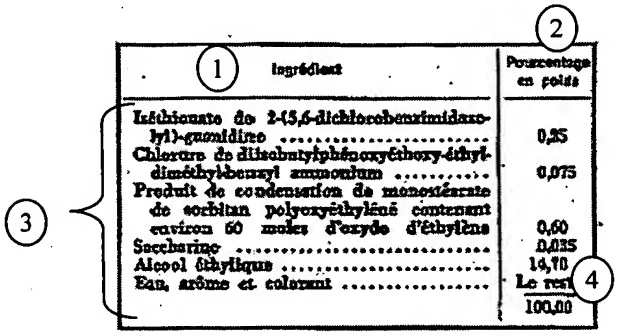
A dental cream essentially containing approximately 0.1-2% 2-(dihalobenzimidazolyl) guanidine, approximately 30-60% of an abrasive (such as talc, chalk, alumina, insoluble sodium metaphosphate, anhydrous dicalcium phosphate), approximately 20-40% of a nontoxic moistener (such as sorbitol, mannitol, glycerol), approximately 1-3% of a nonionic, cationic or anionic detergent (preferably sodium N-lauroyl sarcosinate), and water to make 100%. Furthermore, it is possible to add a compound containing fluorine, such as Na_2FPO_3, NaF, so as to contribute 0.1% fluorine, an opacifier (such as titanium dioxide) in an effective quantity of approximately 0.4%, approximately 1-2% of a substance for putting the debris in suspension (for example, gum tragacanth, carboxymethylcellulose), as well as sweetening, flavoring and coloring agents.

Here is an example of a preferred composition for a chewing tablet:

(1) Ingrédient	Pourcentage en poids (2)
2-(5,6-dichlorobenzimidazolyl)-guanidine ..	1,00
Métaphosphate de sodium insoluble	31,69
Talc	0,50
Phosphate dicalcique (anhydre)	4,03
Mannitol	47,30
Amidon	3,00
Carboxyméthylcellulose (7 MP)	1,25
N-lauroyl sarcosinate de sodium	2,25
Polyéthylène glycol (P.M. 6 000 environ)	5,00
Saccharine	0,25
Stéarate de magnésium	1,25
Arôme, colorant	2,43
(3)	100,00

Key: 1 Ingredient
2 Weight percentage
3 2-(5,6-Dichlorobenzimidazolyl) guanidine
Insoluble sodium metaphosphate
Talc
Dicalcium phosphate (anhydrous)
Mannitol
Starch
Carboxymethylcellulose (7 MP)
Sodium N-lauroyl sarcosinate
Polyethylene glycol (molecular weight approximately 6000)
Saccharin
Magnesium stearate
Flavor, coloring agent

Here is an example of a currently preferred composition for a mouth rinse:

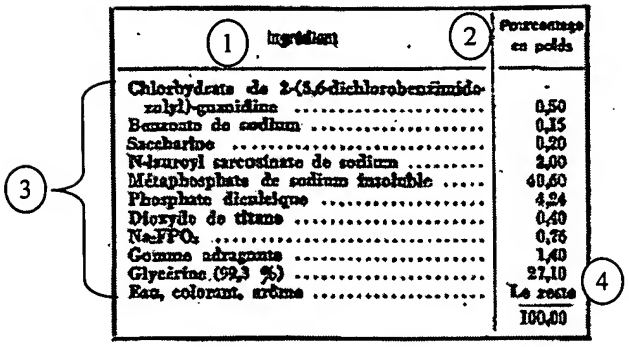


1 Ingrédient	2 Pourcentage en poids
Iséthionate de 2-(5,6-dichlorobenzimidazolyl)-guanidine	0,35
Chlorure de diisobutylphénoxyéthoxy-éthyldiméthylbenzyl ammonium	0,075
Produit de condensation de monostéarate de sorbitan polyoxyéthyléné contenant environ 60 moles d'oxyde d'éthylène	0,60
Saccharine	0,035
Alcool éthylique	14,70
Eau, arôme et colorant	Le reste 4
	100,00

3

Key: 1 Ingredient
2 Weight percentage
3 2-(5,6-Dichlorobenzimidazolyl) guanidine isethionate
Diisobutylphenoxyethoxyethyldimethylbenzylammonium chloride
Product of condensation of polyoxyethylenated sorbitan monostearate containing approximately 60 mol ethylene oxide
Saccharin
Ethyl alcohol
Water, flavor and coloring agent
4 The remainder

Here is an example of a currently preferred composition of a tooth cream:



(1) Ingrédient	(2) Pourcentage en poids
(3) Chlorhydrate de 2-(5,6-dichlorobenzimidazolyl)-guanidine	0,50
Benzoate de sodium	0,15
Saccharine	0,20
N-lauroyl sarcosinate de sodium	2,00
Métaphosphate de sodium insoluble	40,60
Phosphate dicalcique	4,24
Dioxyde de titane	0,40
Na_2FPO_3	0,76
Gomme adragante	1,40
Glycérine (99,3 %)	27,10
Eau, colorant, arôme	(4) Le reste
	100,00

Key: 1 Ingredient
2 Weight percentage
3 2-(5,6-Dichlorobenzimidazolyl) guanidine hydrochloride
Sodium benzoate
Saccharin
Sodium N-lauroyl sarcosinate
Insoluble sodium metaphosphate
Dicalcium phosphate
Titanium dioxide
Na_2FPO_3
Gum tragacanth
Glycerol (99.3%)
Water, coloring agent, flavor
4 The remainder

According to the preceding, it is quite obvious for the specialists that the 2-(dihalobenzimidazolyl) guanidines can be used in the form of free bases or of salts of nontoxic acids, in the form of solutions or suspensions in nontoxic solvents, nontoxic vehicles or nontoxic media. Since the preparation of the 2-(dihalobenzimidazolyl) guanidines is not the object of the present invention, and since their preparation, for example, from halogenated ortho-phenylenediamine and dicyanodiamide, is well known, it will not be described.

Of course, the invention is not limited to the embodiments described, which were only given as examples.

Summary

The invention mainly relates to:

I. A process for improving oral hygiene and inhibiting the formation of dental plaque, said process being remarkable particularly by the following characteristics, considered separately or in combinations:

1. The buccal cavity is put in contact intermittently with a plaque inhibitor which is 2-(dihalobenzimidazolyl) guanidine or one of its salts with a nontoxic acid;

2. The inhibitor is 2-(5,6-dichlorobenzimidazolyl) guanidine and its salts with nontoxic acids, in a concentration of at least 0.01% in a nontoxic vehicle;

3. The inhibitor is presented in the form of a chewing strip containing approximately 0.1-2% 2-(dichlorobenzimidazolyl) guanidine and its salts of nontoxic acids, approximately 30-70% of a compatible abrasive, approximately 30-50% of nontoxic moistener, approximately 0.5-3% of a substance putting the detritus in suspension, approximately 1-3% of a nontoxic detergent, approximately 5% of a binder, approximately 1-2% of a lubricant for a matrix, as well as flavoring agents, coloring agents and sweeteners, to make 100%;

4. The inhibitor is presented in the form of a mouth rinse containing approximately 0.01-5% 2-(dihalobenzimidazolyl) guanidine chosen from 2-(5,6-dichlorobenzimidazolyl) guanidine and its salts of nontoxic acids, approximately 0.5-1% of a nontoxic detergent, a sweetener, aqueous ethyl alcohol, flavoring agents and coloring agents, to make 100%;

5. The plaque inhibitor is a dental cream containing approximately 0.1-2% 2-(dihalobenzimidazolyl) guanidine chosen from 2-(5,6-dichlorobenzimidazolyl) guanidine and its salts of nontoxic acids, 30-60% of an abrasive, approximately 20-40% of a nontoxic moistening agent, approximately 1-3% of a compatible nontoxic detergent, and water, to make 100%;

6. The inhibitor is presented in the form of a chewing strip which contains:
(See 1st table, opposite column.)

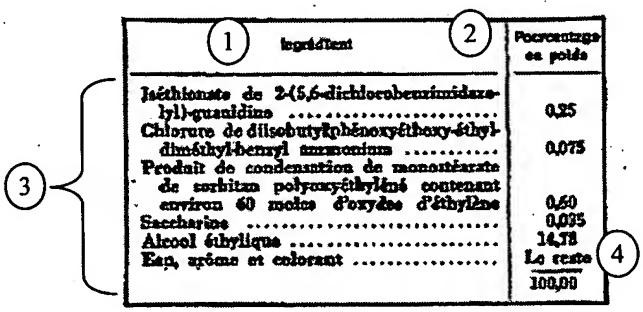
7. The inhibitor is presented in the form of a mouth rinse which contains:
(See 2nd table, opposite column.)

(1) Ingrédient	(2) Pourcentage en poids
2-(5,6-dichlorobenzimidazolyl)-guanidine ..	1,00
Métaphosphate de sodium insoluble	31,69
Talc	0,50
Phosphate dicalcique (anhydre)	4,03
Mannitol	47,80
Amidon	3,00
Carboxyméthylcellulose (7 MP)	1,25
N-lauroyl sarcosinate de sodium	2,25
Polyéthylène glycol (P.M. 6 000 environ)	5,00
Saccharine	0,25
Stéarate de magnésium	1,25
Arôme, colorant	2,48
	100,00

(3)

Key: 1 Ingredient
2 Weight percentage
3 2-(5,6-Dichlorobenzimidazolyl) guanidine
Insoluble sodium metaphosphate
Talc
Dicalcium phosphate (anhydrous)
Mannitol
Starch

Carboxymethylcellulose (7 MP)
Sodium N-lauroyl sarcosinate
Polyethylene glycol (molecular weight approximately 6000)
Saccharin
Magnesium stearate
Flavor, coloring agent

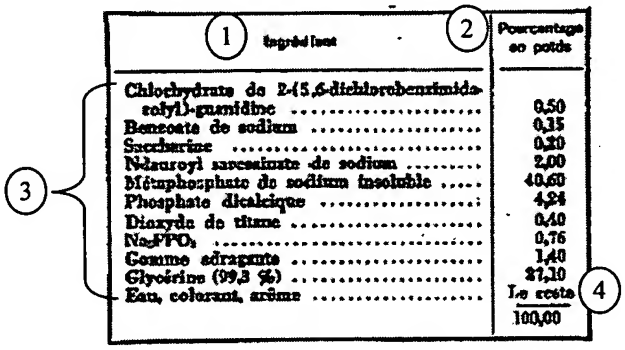


(1) Ingrédient	(2) Pourcentage en poids
Iséthionate de 2-(5,6-dichlorobenzimidazolyl)-guanidine	0,25
Chlorure de diisobutylphénoxyéthoxy-éthyldiméthyl-benzyl ammonium	0,075
Produit de condensation de monostéarate de sorbitan polyoxyéthyléné contenant environ 60 moles d'oxyde d'éthylène	0,60
Saccharine	0,035
Alcool éthylique	14,78
Eau, arôme et colorant	Le reste (4)
	100,00

(3)

Key: 1 Ingredient
2 Weight percentage
3 2-(5,6-Dichlorobenzimidazolyl) guanidine isethionate
Diisobutylphenoxyethoxyethyldimethylbenzylammonium chloride
Product of condensation of polyoxyethylenated sorbitan monostearate containing approximately 60 mol ethylene oxide
Saccharin
Ethyl alcohol
Water, flavor and coloring agent
4 The remainder

8. The inhibitor is presented in the form of a dental cream which contains:



(1) Ingrédient	(2) Pourcentage en poids
Chlorhydrate de 2-(5,6-dichlorobenzimidazolyl)-guanidine	0,50
Benzoate de sodium	0,35
Saccharine	0,20
N-lauroyl sarcosinate de sodium	2,00
Métaphosphate de sodium insoluble	40,60
Phosphate dicalcique	4,24
Dioxyde de titane	0,40
Na_2FPO_3	0,76
Gomme adragante	1,40
Glycérine (99,5 %)	27,10
Eau, colorant, arôme	Le reste (4)
	100,00

(3)

Key: 1 Ingredient
2 Weight percentage
3 2-(5,6-Dichlorobenzimidazolyl) guanidine hydrochloride
Sodium benzoate
Saccharin
Sodium N-lauroyl sarcosinate

Insoluble sodium metaphosphate
Dicalcium phosphate
Titanium dioxide
Na_2FPO_3
Gum tragacanth
Glycerol (99.3%)
Water, coloring agent, flavor
4 The remainder

II. As a new industrial product, a composition for implementation of the process of the invention which is remarkable in that it essentially consists of approximately 0.01-2% of a 2-(dihalobenzimidazolyl) guanidine chosen from 2-(5,6-dihalobenzimidazolyl) guanidines, 2-(4,5-dihalobenzimidazolyl) guanidines, 2-(4,6-dihalobenzimidazolyl) guanidines, 2-(4,7-dihalobenzimidazolyl) guanidines and the salts of these guanidines and nontoxic acids, as well as a nontoxic vehicle.